Search Strategy

FILE 'USPATFULL' ENTERED AT 14:18:21 ON 22 MAR 2001

		E	CHENEBAUX D M B/IN
		E	DELAGNEAU J F H/IN
L1	3	S	E2
		E	GEDELLE S/IN
		E	GADELLE S/IN
L2	1	S	E4
		E	RIEUNIER Y/IN
L3	4004	S	(HIV-1 OR HUMAN IMMUNODEFICIENCY VIRUS TYPE 1)
L4	63	S	L3 AND (GROUP O OR TYPE O OR SUBTYPE O)
L5	17	S	L4 AND GP41
L6	4	S	L5 AND (IMMUNODOMINANT REGION?)
L7	13	S	L5 NOT L6

FILE 'WPIDS' ENTERED AT 14:28:21 ON 22 MAR 2001

		E	CHENEBAUX D/IN
L8	1	S	E4 OR E5
		E	DELAGNEAU J/IN
L9	1	S	E4
L10	0	S	L9 NOT L8
		E	GADELLE S/IN
L11	1	S	E4 OR E5
		E	RIEUNIER F/IN
L12	2	S	E4
L13	1673	S	(HIV-1 OR HUMAN IMMUNODEFICIENCY VIRUS TYPE 1)
L14	16	S	L13 AND (GROUP O OR TYPE O OR SUBTYPE O)
L15	5	S	L14 AND GP41

FILE 'MEDLINE' ENTERED AT 14:34:08 ON 22 MAR 2001

		E	CHENEBAUX D M/AU
L16	6	S	E2
		E	DELAGNEAU J/AU
L17	19	S	E4
		E	GADELLE S/AU
L18	3	S	E3
		E	RIEUNIER F/AU
L19	1	S	E3
L20	30862	S	(HIV-1 OR HUMAN IMMUNODEFICIENCY VIRUS TYPE 1)
L21	129	S	L20 AND (GROUP O OR TYPE O OR SUBTYPE O OR STRAIN O)
L22	27	S	L21 AND (GP41)
L23	6	S	L21 AND (IMMUNODOMINANT REGION)
L24	21	S	L22 NOT L23

L2 ANSWER 1 OF 1 USPATFULL
2000:21368 Immunoenzymatic conjugate, method for its productions, applications thereof.
Cucurou, Christophe, St. Cloud, France
Cognet, Gilles, Yerres, France
Gadelle, Stephane , Bievres, France
Le Sager, Carine, Chatou, France
Pasteur Sanofi Diagnostics, Marnes La Coquette, France (non-U.S. corporation)
US 6027874 20000222
WO 9623226 19960801
APPLICATION: US 1996-714110 19961122 (8)
WO 1996-FR113 19960123 19961122 PCT 371 date 19961122 PCT 102(e) date
PRIORITY: FR 1995-735 19950123
FR 1995-5939 19950518
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Immunoenzymatic conjugate consisting of glycosylated labelling enzymes in copolymer form and substances having immunological activity.

Method for the production of the conjugates according to the invention and use of the said conjugates in diagnostic kits.

L6 ANSWER 1 OF 4 USPATFULL
2000:156965 Peptides for the detection of ***HIV*** - ***1*** ***group*** ***O*** .
De Leys, Robert, Three Bridges, NJ, United States
Zheng, Jian, Raritan, NJ, United States
Ortho-Clinical Diagnostics, Inc., Rochester, NY, United States (U.S. corporation)
US 6149910 20001121
APPLICATION: US 1999-433428 19991104 (9)
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to peptides and their preparation. The peptides each have a sequence that corresponds to the ***immunodominant*** ***region*** of the ***HIV*** - ***1*** ***group*** ***O*** ***gp41*** envelope protein. The sequence is characterized in that it does not correspond to any known naturally occurring ***group*** ***O*** sequence or variant. Furthermore, the peptide binds anti- ***HIV*** - ***1*** ***group*** ***O*** antibodies. There are several uses for the peptides, including the detection of antibodies produced in response to ***HIV*** - ***1*** ***group*** ***O*** infection. The peptides may also be incorporated in mosaics and expressed recombinantly.

L6 ANSWER 2 OF 4 USPATFULL
1999:78540 Rapid assay for simultaneous detection and differentiation of antibodies to HIV groups.
Vallari, Anadruzela S., Libertyville, IL, United States
Hackett, Jr., John R., Libertyville, IL, United States
Hickman, Robert K., Mundelein, IL, United States
Varitek, Jr., Vincent A., Wildwood, IL, United States
Necklaws, Elizabeth C., Grayslake, IL, United States
Golden, Alan M., Wilmette, IL, United States
Brennan, Catherine A., Libertyville, IL, United States
Devare, Sushil G., Northbrook, IL, United States
Abbott Laboratories, Abbott Park, IL, United States (U.S. corporation)

US 5922533 19990713
APPLICATION: US 1997-912129 19970815 (8)
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of performing a rapid assay for the simultaneous detection and differentiation of the analytes ***HIV*** - ***1*** group M. ***HIV*** - ***1*** ***group*** ***O*** and HIV-2 utilizing a sequence specific polypeptide of each analyte as capture reagents. An analytical. device also is provided for performing the method which includes these capture reagents. Also provided is a test kit which includes the analytical device which further can include a positive and negative control.

L6 ANSWER 3 OF 4 USPATFULL
1998:104556 Peptides for ***HIV*** - ***1*** detection.
Bridon, Dominique P., Morton Grove, IL, United States
Sze, deceased, Isaac S.-Y., late of Gurnee, IL, United States by Carolina Luiz, Loch-Hung Leo Sze, Leah Samantha Sze, heirs
Daghfal, David J., Aurora, IL, United States
Jaffe, Keeve D., Trevor, WI, United States
Colpitts, Tracey L., Round Lake, IL, United States
Abbott Laboratories, Abbott Park, IL, United States (U.S. corporation)
US 5800983 19980901
APPLICATION: US 1997-837732 19970422 (8)
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB ***HIV*** - ***1*** peptides having at least one point mutation between position 593 and 611 of the ***HIV*** - ***1*** gp160 amino acid sequence. The point mutation either is at position 604 or 610, or both positions. Immunoassays which utilize these peptides are provided, as well as, diagnostic test kits which contain these peptides.

L6 ANSWER 4 OF 4 USPATFULL
97:36058 Peptides for ***HIV*** - ***1*** detection.
Bridon, Dominique P., Morton Grove, IL, United States
Sze, deceased, Isaac S.-Y., late of Gurnee, IL, United States by Carolina Luiz, Loch-Hung L. Sze, Leah S. Sze, heirs
Daghfal, David J., Aurora, IL, United States
Jaffe, Keeve D., Trevor, WI, United States
Colpitts, Tracey L., Round Lake, IL, United States
Abbott Laboratories, Abbott Park, IL, United States (U.S. corporation)
US 5624797 19970429
APPLICATION: US 1995-472597 19950607 (8)
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB ***HIV*** - ***1*** peptides having at least one point mutation between position 593 and 611 of the ***HIV*** - ***1*** gp160 amino acid sequence. The point mutation either is at position 604 or 610, or both positions. Immunoassays which utilize these peptides are provided, as well as, diagnostic test kits which contain these peptides.

L7 ANSWER 9 OF 13 USPATFULL
1998:98770 HIV-3 retrovirus antigen compositions.
De Leys, Robert, Grimbergen, Belgium
Vanderborght, Bart, Geel, Belgium
Saman, Eric, St. Niklaas, Belgium
Van Heuverswyn, Hugo, Laarne, Belgium

Innogenetics N.V., Ghent, Belgium (non-U.S. corporation)
US 5795743 19980818
APPLICATION: US 1995-486836 19950607 (8)
PRIORITY: EP 1988-109200 19880609
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Described is a new variety of retrovirus designated HIV-3 samples of which are deposited in the European Collection of Animal Cell Cultures (ECACC) under V88060301. Further described are antigens obtained from the virus, particularly proteins p12, p16, p25 and glycoproteins ***gp41*** and gp120 to be used in the diagnosis of ARC or AIDS caused by HIV-3. Immunogenic compositions to be used as vaccines contain an envelope glycoprotein of HIV-3 such as ***gp41*** or gp120.

L7 ANSWER 7 OF 13 USPATFULL
1998:134790 Peptides derived from a retrovirus of the HIV group and their use.
Brust, Stefan, Marburg-Michelbach, Germany, Federal Republic of
Knapp, Stefan, Marburg, Germany, Federal Republic of
Gerken, Manfred, Marburg, Germany, Federal Republic of
Guertler, Lutz G., Munich, Germany, Federal Republic of
Dade Behring Marburg GmbH, Marburg, Germany, Federal Republic of (non-U.S. corporation)
US 5830634 19981103
APPLICATION: US 1995-394021 19950223 (8)
PRIORITY: DE 1994-4405810 19940223
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Immunologically active peptides which are derived from a novel immunodeficiency virus which has the designation MVP5180/91 are described. A diagnostic composition containing such a peptide and methods of detecting an antibody against a retrovirus that causes immune deficiency using such diagnostic composition are also described. A kit containing the immunologically active peptides is also described. An immunogen and method of immunizing a mammal against HIV infection using the immunologically active peptides is described. DNA encoding the peptides and methods of detecting nucleic acids encoding HIV viruses are also described.

L7 ANSWER 6 OF 13 USPATFULL
1999:4316 Methods for detecting antibodies against HIV-3 retrovirus [and its use].
De Leys, Robert, Grimbergen, Belgium
Vanderborght, Bart, Geel, Belgium
Saman, Eric, Niklaas, Belgium
Van Heuverswyn, Hugo, Laarne, Belgium
Innogenetics N.V., Ghent, Belgium (non-U.S. corporation)
US 5858647 19990112
APPLICATION: US 1995-474360 19950607 (8)
PRIORITY: EP 1988-109200 19880609
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Described is a new variety of retrovirus designated HIV-3, samples of which are deposited in the European Collection of Animal Cell Cultures (ECACC) under V88060301. Further described are antigens obtained from the virus, particularly proteins p12, p16, p25 and glycoproteins ***gp41*** and gp120 to be used in the diagnosis of ARC or AIDS caused by HIV-3. The methods to detect antibodies against HIV-3 retrovirus in a biological fluid involve contacting the suspect body fluid with a

composition containing one or more of the proteins or glycoproteins of HIV-3 or with a lysate of the virus, or with an antigen possessing epitopes common to HIV-3, and detecting the immunological conjugate formed between the anti-HIV-3 antibodies and the antigen(s) used.

L7 ANSWER 4 OF 13 USPATFULL

2000:24443 ***Group*** ***O*** ***HIV*** - ***1*** , fragments of such viruses, and uses thereof.

Simon, Fran.cedilla.ois, Paris, France
Saragosti, Sentob, Boulogne-Billancourt, France
Loussert-Ajaka, Ibtissam, Sartrouville, France
Ly, Thoai-Duong, Rueil-Malmaison, France
Chaix-Baudier, Marie-Laure, Paris, France
Institut National de la Sante et de la Recherche Medical-Inserm, Paris Cedex, France (non-U.S. corporation)Assistance Publique-Hopitaux de Paris, Paris, France (non-U.S. corporation)
US 6030769 20000229
WO 9627013 19960906
APPLICATION: US 1997-894699 19971201 (8)
WO 1996-FR294 19960226 19971201 PCT 371 date 19971201 PCT 102(e) date
PRIORITY: FR 1995-2236 19950227
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Group ***HIV*** - ***1*** retrovirus strains, particularly the strains known as BCF02, BCF01, BCF06, BCF07, BCF08, BCF11, BCF03, BCF09, BCF12, BCF13 and BCF14, fragments of said retroviruses, and the uses thereof as a diagnostic reagent and as an immunogen, are disclosed.

L8 ANSWER 1 OF 1 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1998-583190 [49] WPIDS
DNC C1998-174411
TI New synthetic peptide(s) - useful for, e.g. detecting infection by human immune deficiency virus of group O.
DC B04 D16
IN ***CHENEBAUX, D M B*** ; DELAGNEAU, J H; GADELLE, S J X; RIEUNIER, F Y; DELAGNEAU, J F H; UNIER, F Y; ***CHENEBAUX, D M*** ; DELAGNEAU, J; GADELLE, S J
PA (SNFI) PASTEUR SANOFI DIAGNOSTICS SA; (SNFI) PASTEUR SANOFI DIAGNOSTICS
CYC 84
PI WO 9845323 A1 19981015 (199849)* FR 55p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
FR 2761993 A1 19981016 (199849)
AU 9873386 A 19981030 (199911)
FR 2775287 A1 19990827 (199941)
ZA 9802996 A 19991229 (200006) 59p
NO 9904929 A 19991208 (200009)
EP 973802 A1 20000126 (200010) FR
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT RO SE SI
CZ 9903575 A3 20000614 (200037)
BR 9809078 A 20000801 (200043)
CN 1256695 A 20000614 (200048)
ADT WO 9845323 A1 WO 1998-FR691 19980406; FR 2761993 A1 FR 1997-4356 19970409; AU 9873386 A AU 1998-73386 19980406; FR 2775287 A1 FR 1998-2212 19980224; ZA 9802996 A ZA 1998-2996 19980408; NO 9904929 A WO 1998-FR691 19980406, NO 1999-4929 19991008; EP 973802 A1 EP 1998-920571 19980406, WO 1998-FR691 19980406; CZ 9903575 A3 WO 1998-FR691 19980406, CZ 1999-3575 19980406; BR 9809078 A BR 1998-9078 19980406, WO 1998-FR691 19980406; CN 1256695 A CN 1998-805202 19980406
FDT AU 9873386 A Based on WO 9845323; EP 973802 A1 Based on WO 9845323; CZ 9903575 A3 Based on WO 9845323; BR 9809078 A Based on WO 9845323
PRAI FR 1998-2212 19980224; FR 1997-4356 19970409

AB WO 9845323 A UPAB: 19981210
Synthetic peptides (A), of 13-33 amino acids (aa) when monomeric or 26-66 when dimeric (either linear or cyclised by Cys-Cys-disulphide bonds), have formula (I): Delta -Z-Trp-Gly-Cys-th-Cys-Tyr-Ser- Omega (I) Delta = biotinyl, biocytinyl, hydrogen, acetyl, aliphatic chain (preferably 1-6 C alkyl, or 2-6 C alkenyl or aminoalkylcarbonyl) , optionally containing 1 or 2 mercapto, formyl or amino groups; Z = x1-(Ser, Gln or Asn)-x2; x1 = 0-9 aa; x2 = 0-5 aa; th = -AA1-AA2-AA3-AA4-AA5-; AA1 = Lys, Arg or Thr; AA2 = Gly or Asn; AA3 = Lys, Arg or ornithine (Orn); AA4 = Leu, Ala, Ile or Gln; AA5 = Ile, Val, Leu, Thr, norleucine (Nle) or norvaline (Nva); provided that AA1-AA5 is not Lys-Gly-Lys-Leu-(Ile or Val); Omega , attached to carbonyl of Ser, = hydroxy, amino, 1-6 C alkoxy, Val- - phi , -Z-Trp-Gly-Cys-th-Cys-Tyr-Thr-Ser- psi , or Val- -Z-Trp-Gly-Cys-th-Cys-Tyr-Thr-Ser-Val- - psi ; , optionally absent, = AA6-Trp-(Asn or His)-AA7-AA8; AA6 = aa other than Lys; AA7 = any aa; AA8 = Ser or Thr; phi , attached to carbonyl on AA8,Val or Ser, = OH, amino or 1-6 C alkoxy.

USE - (I), or their mixtures, are useful as immunological reagents for detecting infection by group O human immune deficiency virus (HIV). They represent variable sequences connected around short highly conserved sequences present in isolates of this group.

ADVANTAGE - (A) are better diagnostic agents than synthetic peptides that carry the immunodominant epitopes of gp41 of group O viruses.
Dwg.0/0

L15 ANSWER 1 OF 5 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-656164 [63] WPIDS
DNC C2000-198581
TI Synthetic peptides useful for preventing and treating HIV infection in mammals, comprising a conformationally constrained portion and a portion with continuous stretch of amino acids of predicted secondary structure.
DC B04 D16
IN BERNSTEIN, D; CHOWDHURY, A; KOZHICH, A; MOTSENBOCKER, M
PA (BERN-I) BERNSTEIN D; (CHOW-I) CHOWDHURY A; (KOZH-I) KOZHICH A; (MOTS-I) MOTSENBOCKER M
CYC 92
PI WO 2000058438 A2 20001005 (200063)* EN 69p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000037740 A 20001016 (200106)
ADT WO 2000058438 A2 WO 2000-US8232 20000329; AU 2000037740 A AU 2000-37740 20000329
FDT AU 2000037740 A Based on WO 200058438
PRAI US 1999-126938 19990329

AB WO 200058438 A UPAB: 20001205
NOVELTY - A peptide (I) 16 to 75 amino acids long comprising a first conformationally constrained portion (P1) 5 to 13 amino acids long with a cross-linked group of a human immuno-deficiency virus (HIV) envelope protein that induces neutralizing antibodies, and a second portion (P2) comprising a continuous stretch of at least 5 amino acids having a predicted secondary structure, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a pharmaceutical composition comprising (I) useful for prophylactic or therapeutic treatment of a mammal at risk for or infected with HIV;

(2) preparation of (I);

(3) a peptide (II) having a modification of a sequence from an envelope protein of a virus that fuses with a host cell in a pH independent manner, where the modification comprises replacement of an enhancing group of the envelope protein with a neutralizing group from the same virus;

(4) designing a peptide to elicit the production of neutralizing antibodies targeted to a virus that fuses with a host cell in a pH-independent manner, comprising obtaining a sequence of an envelope protein of the virus and replacing an enhancing group of the envelope protein sequence with a neutralizing group from the same virus.

ACTIVITY - Anti-HIV.

MECHANISM OF ACTION - Vaccine.

No supporting data is given.

USE - (I) is useful as vaccine for prophylactic or therapeutic treatment of a mammal for human immuno-deficiency virus (HIV) infection (claimed).

ADVANTAGE - (I) is useful for vaccinating against viruses that fuse their host in a pH independent manner.
Dwg.0/0

L15 ANSWER 2 OF 5 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-086953 [07] WPIDS
CR 1999-494079 [38]
DNC C2000-024237
TI Improving properties of peptides for use as diagnostic antigens or for preventing or treating infections.
DC B04 D16
IN BERNSTEIN, D; CHOWDHURY, M A; MOTSENBOCKER, M A
PA (PEPT-N) PEPTIDE SOLUTIONS INC
CYC 86
PI WO 9962945 A2 19991209 (200007)* EN 82p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9945463 A 19991220 (200021)
ADT WO 9962945 A2 WO 1999-US12446 19990604; AU 9945463 A AU 1999-45463 19990604
FDT AU 9945463 A Based on WO 9962945
PRAI WO 1999-US1726 19990128; US 1998-88229 19980605; US 1998-98705 19980901; US 1998-100422 19980915

AB WO 9962945 A UPAB: 20000502
NOVELTY - A peptide useful for detecting human immunodeficiency virus (***HIV***)- ***1*** ***group*** ***O*** infection, having a length of 16-100 residues and comprising a core sequence fully defined in the specification, is new.

DETAILED DESCRIPTION - The core sequence has the sequence X1-X1-X1-X2-X3-X1-X4-W-G-C-X2-G-X2-X4-X3-C

X1 = N, Q, G, S, T or A
X2 = R or K
X3 = N, Q, G, S, T, H, A, L, I, V, P or M
X4 = N, Q, G, S, T, H, A, P or M

INDEPENDENT CLAIMS are also included for the following:

(1) a peptides useful for detecting ***HIV*** - ***1*** ***group*** ***O*** infection, having a length of 26-100 amino acids, comprising the core sequence X-X1-X1-X1-X2-X3-X1-X1-W-G-C-X2-X1-X3-C-Y-X4-X4-X3-X2-W-X1-X5, where X is a helix of at least 5 amino acids, X1 is N, Q, G, S, T, D, N, H or A, X2 is R, K, P, or E, X3 is I, L or V, X4 is T, S or A and X5 is at least one amino acid;

(2) a peptide useful for detecting ***HIV*** - ***1*** ***group*** ***O*** infection, having 36-100 amino acids, comprising a core sequence selected from 18 sequences fully defined in the specification, and derivatives containing one or more conservative amino acid substitutions;

(3) a peptide (Ib) for detecting ***HIV*** - ***1*** Infection, having a sequence of at least 35 aa from the ***gp41*** immunomodulatory region and including at least 5 aa in a alpha -helix structure (as defined by Chou-Fasman calculations) at the N-terminal side of the immunomodulatory region;

(4) reagent for detecting anti-HIV antibodies in blood comprising a dried antigen that, when rewetted, reacts with antibodies in patients with ***group*** ***O*** or M infections, the antigen containing 16-50 aa;

(5) method for detecting ***HIV*** - ***1*** ***Group*** ***O*** infection by incubating blood (or its derivative) with (Ia), then detecting binding of (Ia) to antibodies;

(6) kits for method (5);

(7) diagnostic test peptide antigen (Ag), for detecting an infectious

agent, comprising a natural sequence modified by replacing at least one aa1 by an aa2;

(8) peptide (II) of 26-100 aa, including a central portion of at least 16 aa corresponding to an immunodominant region, with at least one aa at each end of this region, that is chemically synthesized and has at least one aa1 in the immunodominant region replaced by aa2;

(9) modified peptide (III) for treating or preventing infection that has at least one L, I or V in a natural sequence replaced by A, S, T, G or N; and

(10) peptide (IV) for detecting hepatitis C infection containing 24-100 aa and one of several specified core sequences (or their derivatives with one or more conservative aa substitutions).

ACTIVITY - Antiviral.

MECHANISM OF ACTION - The methods increase structural stability of epitopes within the peptide, such that these react better with antibodies.

USE - Modified (I) are used to detect infectious agents (specifically human immune deficiency virus-1 (***HIV*** - ***1***), including specific detection of ***Group*** ***O*** viruses; human T-cell lymphotropic virus-I or -II; hepatitis C and the causative agent of syphilis) and for prevention or treatment of infections (e.g. as vaccines, or where expressed from a transgene). More generally almost any peptide can be similarly modified, e.g. cytokines and interferons; major histocompatibility complex antigens; hormones; growth factors; tumor markers or suppressors etc., or antigens from many other pathogens.

ADVANTAGE - Modified (I) are cross-reactive with a wide range of mutant forms of an antigen, so produce fewer false assay results, especially when used for detecting pathogens that mutate rapidly. They may also have better water solubility and immunoreactivity compared with wild-type (I).

Dwg.0/5

L15 ANSWER 3 OF 5 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-551081 [46] WPIDS
DNN N1999-407802 DNC C1999-160767
TI Confirming infection by detecting antibodies against two different antigens, particularly from human immune deficiency virus, hepatitis C or syphilis.
DC B04 D16 S03
IN BERNSTEIN, D; CHILDS, M A; CHOWDURY, M A; LOVCHIK, J
PA (UVHE-N) UNIVERSAL HEALTH-WATCH INC; (UVHE-N) UNIVERSAL HEALTHWATCH INC
CYC 84
PI WO 9945395 A1 19990910 (199946)* EN 42p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9927908 A 19990920 (200007)
EP 993615 A1 20000419 (200024) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9945395 A1 WO 1999-US4175 19990226; AU 9927908 A AU 1999-27908 19990226; EP 993615 A1 EP 1999-908487 19990226, WO 1999-US4175 19990226
FDT AU 9927908 A Based on WO 9945395; EP 993615 A1 Based on WO 9945395
PRAI US 1998-76748 19980304

AB WO 9945395 A UPAB: 19991110
NOVELTY - Infection by a specific microbe (A) is confirmed by test device comprising housing with opening, holding absorbent pad (AP) and reagent layer (RL), in contact with AP and aligned with opening. RL contains antigens from (A), immobilized in separate regions. A blood sample is

applied through the opening, and wash fluid supplied. Detection of antibody-antigen reactions in RL confirms the infection.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) the device; and

(2) improvement to a device for detecting microbes by replacing a recombinant antigen with two or more allelic peptides that cross-react with an immunodominant region of a microbial protein.

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - The method is especially used to confirm infection by human immune deficiency virus (HIV), syphilis and/or hepatitis C virus, but can be used more generally to detect a wide range of bacteria, viruses and other parasites.

ADVANTAGE - The method is rapid (contrast Western blotting), easy to use by untrained personnel, inexpensive and provides information on the subtype of HIV present. Only a single drop of blood is needed and several different pathogens may be detected simultaneously. Where the antigens are different allelic variants of the same protein, a wide range of epitopes (strains) can be detected.

Dwg.0/3

L15 ANSWER 4 OF 5 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-494079 [41] WPIDS
DNN N1999-368042 DNC C1999-144776
TI Improved peptide antigens for HIV diagnostic testing and therapy.
DC B04 D16 S03
IN BERNSTEIN, D; CHOWDHURY, M A
PA (UVHE-N) UNIVERSAL HEALTH-WATCH INC; (UVHE-N) UNIVERSAL HEALTHWATCH INC
CYC 82
PI WO 9938887 A1 19990805 (199941)* EN 53p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9923453 A 19990816 (200002)
ADT WO 9938887 A1 WO 1999-US1726 19990128; AU 9923453 A AU 1999-23453 19990128
FDT AU 9923453 A Based on WO 9938887
PRAI US 1998-72981 19980129; US 1998-72863 19980128

AB WO 9938887 A UPAB: 20000209

NOVELTY - A peptide sequence, chosen to differ from the accepted consensus sequences by at least 25%, has a broader antibody specificity than peptides derived from ***Human*** ***immunodeficiency*** ***virus*** ***type*** ***1*** (***HIV*** - ***1***).

DETAILED DESCRIPTION - A peptide (I), between 26 and 100 amino acids (aa) long that substantially reacts with group M and ***group*** ***O*** ***HIV*** - ***1*** test specimens, and that comprises a 16 aa long immunodominant region comprises a sequence selected from the two sequences (Ia) or (Ib) (given in the specification).

INDEPENDENT CLAIMS are also included for the following:

(1) a reagent for immunological detection of anti-HIV antibody in a blood sample, comprising a dried antigen that, upon rewetting with water or a clinical sample, substantially reacts with antibodies from patients exposed to ***HIV*** - ***1*** group M virus and with antibodies from patients exposed to ***HIV*** - ***1*** ***group*** ***O*** viruses, wherein the antigen is between 26-40 aa long a sequence selected from (Ib);

(2) a composition for stimulating the formation of antibodies against

HIV - ***1*** virus comprising a peptide as above and a powder or liquid carrier;

(3) a peptide between 26 and 100 a long that substantially reacts with group M and ***group*** ***O*** ***HIV*** - ***1*** test specimens, produced by:

(i) selecting an M consensus sequence of at least 16 aa long from the immunodominant region of ***gp41*** envelope protein of ***HIV*** - ***1*** ;

(ii) deriving a new aa sequence from this that diverges by at least 25% by selecting alternative aa from (Ia); and

(iii) synthesizing a peptide having the derived sequence, where the same method can be used, using the sequence in (Ib) (in this case the peptide is between 30-40 aa long, and is especially 20 aa long and comprises position numbers 587 to 609 (Ib)), and

(4) a composition comprising the peptide of (3), especially comprising a peptide which differs from the sequence RARLQALETLIQNQQRLNLWGCKGKLICYTSVKWNT by at least 2, 3 or 4 aa.

ACTIVITY - Antigenic; immunogenic.

MECHANISM OF ACTION - None given.

USE - The peptides and polynucleotides encoding them, are useful as vaccines for protection against ***HIV*** - ***1*** or HIV-2 infection. The compositions and methods may also be used for ex vivo therapy in the treatment of ***HIV*** - ***1*** infection.

ADVANTAGE - The problem of ***HIV*** - ***1*** protein diversity affects not only diagnostic testing for exposure to HIV, but also hinders the development of therapies and prophylactics to prevent HIV infection. The peptides of the invention eliminate the problems of the prior art by providing a paradigm. The peptides reduce or eliminate the problems of insufficient stimulation reactivity of peptide antigen with HIV antibody, HIV mutation and variation, insufficient reactivity, and awkward production requirements.

Dwg.0/2

L15 ANSWER 5 OF 5 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1997-052229 [05] WPIDS
DNN N1997-042857 DNC C1997-017380
TI Hybrid polypeptide(s) comprising ***HIV*** - ***1*** sub-type B immuno dominant region - contg. 1 or more specific amino acid substitutions critical for detecting ***HIV*** - ***1*** sub-***type*** ***O*** , useful in immunoassay for detecting HIV antibodies.
DC A96 B04 D16 J04 S03
IN BRIDON, D P; COLPITTS, T L; DAGHFAL, D J; JAFFE, K D; SZE, I S
PA (ABBO) ABBOTT LAB
CYC 21
PI WO 9640763 A2 19961219 (199705)* EN 34p
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP
WO 9640763 A3 19970206 (199722)
US 5624797 A 19970429 (199723)
EP 832113 A2 19980401 (199817) EN
R: BE CH DE ES FR GB IT LI
US 5800983 A 19980901 (199842)
JP 11507635 W 19990706 (199937) 37p
ADT WO 9640763 A2 WO 1996-US9655 19960607; WO 9640763 A3 WO 1996-US9655 19960607; US 5624797 A US 1995-472597 19950607; EP 832113 A2 EP 1996-921412 19960607, WO 1996-US9655 19960607; US 5800983 A Cont of US 1995-472597 19950607, US 1997-837732 19970422; JP 11507635 W WO 1996-US9655 19960607, JP 1997-501929 19960607
FDT EP 832113 A2 Based on WO 9640763; JP 11507635 W Based on WO 9640763
PRAI US 1995-472597 19950607; US 1997-837732 19970422

AB WO 9640763 A UPAB: 19970129
Polypeptide having a point mutation in the ***HIV*** - ***1*** sub-type B immunodominant region (IDR) at position 604 and/or 610, is claimed. Also claimed are: (1) immunoassay to detect the pressure of HIV antibodies in a test sample, comprising: (a) contacting the test sample with a solid phase to which a ***HIV*** - ***1*** polypeptide having a point mutation between positions 593 and 611 has been attached, to form a 1st mixt., and incubating the 1st mixt. for a time and under conditions sufficient to form polypeptide/antibody complexes; (b) contacting the complexes with an indicator reagent comprising a member of a specific binding pair attached to signal generating cpd. capable of generating a measurable signal, to form a 2nd mixt., and incubating the 2nd mixt. for a time and under conditions sufficient to form polypeptide/antibody/indicato r reagent complexes; and (c) determining the presence of HIV antibodies in the test sample by detecting te measurable signal; and (2) an immunoassay for detecting HIV antibody in test sample, comprising contacting the test sample with a ***HIV*** - ***1*** , polypeptide and detecting the presence of the antibody, where the improvement comprises utilising a polypeptide having at least 1 point mutation between positions 593 and 611 of the ***HIV*** - ***1*** gp 160 sequence.

USE - The polypeptides which are hybrid polypeptides comprising the ***gp41*** IDR or ***HIV*** - ***1*** sub-type B contg. 1 or more specific amino acid substitutions critical for the detection of ***HIV*** - ***1*** sub- ***type*** ***O*** , can be used for the detection of HIV antibodies (kit provided).

The hybrid polypeptides are capable of reacting with the anti- ***HIV*** - ***1*** sub- ***type*** ***O*** antibodies present in a panel of confirmed ***HIV*** - ***1*** sub- ***type*** ***O*** test samples, some of which were not reactive when the unmodified sub-type B sequence was used.
Dwg.1/5

L17 ANSWER 4 OF 19 MEDLINE
91119249 Document Number: 91119249. Criteria for the selection of a solid phase to be used in immunoassays. ***Delagneau J F*** ; Masseyeff R. (Diagnostics Pasteur, Marnes-La-Coquette.) ANNALES DE BIOLOGIE CLINIQUE, (1990) 48 (7) 467-71. Journal code: 4ZS. ISSN: 0003-3898. Pub. country: France. Language: English.

AB Heterogeneous immunoassays are very sensitive and only limited in terms of performance by non specific binding. They require separation of free from bound fractions and concomitant use of a solid phase coated with an immunoreactive component (i.e. immunosorbent). The improvement of these key immunosorbents is crucial and involves a great deal of expertise and capabilities. Specifications differ according to procedure (e.g. capture or competitive assay). Each routinely used solid phase, such as polystyrene wells, porous membrane or dispersible microbeads, presents specific performance characteristics, advantages, and drawbacks. Among the tasks to be implemented are optimization of the spatial orientation of immunological reagents, selection of the surface neutral hydrophilic support, acceleration of reactions by increasing the reactive surface area of the supports, streamlining and simplification of procedural steps. These various aspects are abundantly described and emphasized here.

L23 ANSWER 3 OF 6 MEDLINE
1998163276 Document Number: 98163276. Reactivity of a new ***HIV*** - ***1*** ***group*** ***O*** third generation A- ***HIV*** - ***1*** /-2 assay with an unusual ***HIV*** - ***1*** seroconversion panel and ***HIV*** - ***1*** ***group*** ***O*** /group M subtyped samples. van Binsbergen J; Keur W; v.d. Graaf M; Siebelink A; Jacobs A; de Rijk D; Toonen J; Zekeng L; Afane Ze E; Gurtler L G. (Organon Teknika, Boxtel, The Netherlands.) JOURNAL OF VIROLOGICAL METHODS, (1997 Dec) 69 (1-2) 29-37. Journal code: HQR. ISSN: 0166-0934. Pub. country: Netherlands. Language: English.

AB It was shown previously that about 97% of the anti- ***HIV*** - ***1*** ***group*** ***O*** strain-positive samples were detected by crossreaction with native ***HIV*** - ***1*** gp160 (Van Binsbergen et al., Evaluation of a new third generation anti- ***HIV*** - ***1*** /anti-HIV-2 assay with increased sensitivity for ***HIV*** - ***1*** ***group*** ***O*** , J. Virol. Methods 60 (1996) 131-137). Fourteen out of 17 new anti- ***HIV*** - ***1*** ***group*** ***O*** positive samples, selected with the Enzygnost ***HIV*** - ***1*** /2 plus assay, were already reactive when tested with ***HIV*** - ***1*** gp160. When tested by the Vironostika HIV Uni-Form II plus O microELISA all 17 samples were reactive, demonstrating the necessity to implement an ***HIV*** - ***1*** ***group*** ***O*** -specific antigen in the assay. On the other hand, it was surprisingly found that 40 out of 43 (93%) of anti- ***HIV*** - ***1*** group M-positive samples, belonging to strain A, B, C, D, E or F, were detected by crossreaction with the ***HIV*** - ***1*** ***group*** ***O*** (strain ANT70) synthetic peptide incorporated in the Vironostika HIV Uni-Form II plus O. Only ***HIV*** - ***1*** subtype D-positive samples did not react with this peptide, presumably because of the presence of a histidine residue in the ***immunodominant*** ***region*** of ***HIV*** - ***1*** subtype D gp41. Both crossreactions make the Vironostika HIV Uni-Form II plus O microELISA also sensitive for anti- ***HIV*** - ***1*** -positive samples originating from different geographical regions and resulting from different ***HIV*** - ***1*** subtype infections. With an unusual seroconversion panel in which p24 Ag was present persistently, many anti- ***HIV*** - ***1*** /-2 assays produce alternating positive/negative results in anti-HIV antibody-positive

bleeds. It was shown that the use of viral p24 and gp160 in a direct sandwich, allowing detection of anti-HIV IgG and IgM, explains the identification of all anti-HIV-positive bleeds by the Vironostika HIV Uni-Form II plus O. The high sensitivity of the plus O assay was confirmed with clinical samples of a so-called anti- ***HIV*** - ***1*** low titer panel. The specificity of the Vironostika HIV Uni-Form II plus O determined in five blood transfusion centers, based on 135070 tests, was 99.97%.

L23 ANSWER 4 OF 6 MEDLINE
97418745 Document Number: 97418745. Diversity of the immunodominant epitope of gp41 of ***HIV*** - ***1*** ***subtype*** ***O*** and its validity for antibody detection. Eberle J; Loussert-Ajaka I; Brust S; Zekeng L; Hauser P H; Kaptue L; Knapp S; Damond F; Saragosti S; Simon F; Gurtler L G. (Pettenkofer Institute, University of Munchen, Germany.) JOURNAL OF VIROLOGICAL METHODS, (1997 Aug) 67 (1) 85-91. Journal code: HQR. ISSN: 0166-0934. Pub. country: Netherlands. Language: English.

AB The immunodominant regions of the gp41 from 13 ***HIV*** - ***1*** ***subtype*** ***O*** strains from Cameroon, 11 from France and one from Germany were sequenced. The amino acid sequences were compared to those of the 3 published ***HIV*** - ***1*** ***subtype*** ***O*** isolates, ANT70, MVP-5180 and VAU. All ***HIV*** - ***1*** ***subtype*** ***O*** isolates had a very conserved amino acid sequence in this region and showed a ***subtype*** ***O*** specific structure. Within the cysteine loop there was a positive charge of two basic amino acids, arginine and lysine. Only two strains (CM.6778 and CM.8161) showed an acidic amino acid in this loop. None of the isolates showed the same amino acid sequence in this ***immunodominant*** ***region*** . A 25 residue peptide from the immunodominant domain of gp41 of the MVP-5180 strain was synthesized, cycled to form the cysteine-loop and coated to microtiter plates. Antibody binding was detected by indirect ELISA using an enzyme labeled anti-human IgG. Out of 111 anti- ***HIV*** - ***1*** positive specimens, collected mainly from Cameroonian HIV infected patients, only 10 were not reactive in this assay. The 42 anti- ***HIV*** - ***1*** ***subtype*** ***O*** positive specimens gave all a reaction above cut off. Despite the diversity found in the amino acid sequences within the 25 isolates a peptide-based indirect ELISA representing the immunodominant epitope of the strain MVP-5180 successfully detected all the anti-HIV-O sera so far tested, pointing to the importance of adding such a peptide for correct identification of ***HIV*** - ***1*** ***subtype*** ***O*** infected patients, while some assays without HIV-O specific antigens partially fail to detect all anti-HIV-O specimens.

L23 ANSWER 5 OF 6 MEDLINE
97340911 Document Number: 97340911. Sequence of gp41env ***immunodominant*** ***region*** of HIV type 1 ***group*** ***O*** from west central Africa. Brennan C A; Hackett J Jr; Zekeng L; Lund J K; Vallari A S; Hickman R K; Gurtler L; Kaptue L; Von Overbeck J; Hampl H; Devare S G. (Viral Discovery, Abbott Laboratories, North Chicago, Illinois 60064, USA.) AIDS RESEARCH AND HUMAN RETROVIRUSES, (1997 Jul 1) 13 (10) 901-4. Journal code: ART. ISSN: 0889-2229. Pub. country: United States. Language: English.

L23 ANSWER 6 OF 6 MEDLINE
97001626 Document Number: 97001626. Evaluation of a new third generation anti- ***HIV*** - ***1*** /anti-HIV-2 assay with increased sensitivity for ***HIV*** - ***1*** ***group*** ***O*** . van Binsbergen J; de Rijk D; Peels H; Dries C; Scherders J; Koolen M; Zekeng L; Gurtler L G. (Organon Teknika, Boxtel, The Netherlands.) JOURNAL OF VIROLOGICAL

METHODS, (1996 Jul) 60 (2) 131-7. Journal code: HQR. ISSN: 0166-0934. Pub. country: Netherlands. Language: English.

AB Although the ***HIV*** - ***1*** ***group*** ***O*** virus found in two persons of Cameroonian origin has been described in 1990 (De Leys et al., 1990), sera from ***group*** ***O*** infected individuals became available only recently. Several studies showed that some of the anti- ***HIV*** - ***1*** /HIV-2 screening tests failed to detect all of these samples (Loussert-Ajaka et al., 1994; Simon et al., 1994; Schable et al., 1994; Gurtler et al., 1995). In the current version of an anti- ***HIV*** - ***1*** /anti-HIV-2 screening assay, namely the Vironostika HIV Uni-Form II, an HIV-O specific peptide was introduced in order to improve ***HIV*** - ***1*** ***group*** ***O*** reactivity. The peptide was derived from the ***immunodominant*** ***region*** of ***HIV*** - ***1*** ***group*** ***O*** gp41 strain ANT70. All 30 anti- ***HIV*** - ***1*** ***group*** ***O*** sera were detected by the so-called plus O assay, while 29 samples of this panel were positive the current assay. The sensitivity of the plus O assay for anti- ***HIV*** - ***1*** and anti-HIV-2 positive samples is identical to that of the reference test without ***HIV*** - ***1*** ***group*** ***O*** peptide. The clinical specificity of the HIV Uni-Form II plus O assay is improved to > or = 99.92% by an adjustment of the coat concentration of ***HIV*** - ***1*** p24 (to avoid false positive p24 only reactions) without affecting sensitivity of the assay. The specific reaction of an ***HIV*** - ***1*** ***group*** ***O*** specific rabbit serum for quality control purposes is presented.

L24 ANSWER 1 OF 21 MEDLINE
2000454551 Document Number: 20414627. Presence of diverse ***human*** ***immunodeficiency*** ***virus*** ***type*** ***1*** viral variants in Cameroon. Fonjungo P N; Mpoudi E N; Torimiro J N; Alemnji G A; Eno L T; Nkengasong J N; Gao F; Rayfield M; Folks T M; Pieniazek D; Lal R B. (HIV/AIDS and Retrovirology Branch, Division of AIDS, STD and TB Laboratory Research, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333, USA.) AIDS RESEARCH AND HUMAN RETROVIRUSES, (2000 Sep 1) 16 (13) 1319-24. Journal code: ART. ISSN: 0889-2229. Pub. country: United States. Language: English.

AB Phylogenetic analysis of the ***gp41*** region of 123 ***HIV*** - ***1*** -seropositive specimens from Cameroon showed that 89 were subtype A (71% of these sequences were IbNg-like), 12 (10%) were subtype D, 11 (9%) were subtype G, 5 (4%; closely related to subtype F2) were subtype F, 1 was subtype H, 2 (1.6%) remained unclassifiable, while 3 were ***group*** ***O*** . Further analysis of the two unclassifiable specimens in gag(p24), pol(prot), and env (C2V3 or ***gp41***) showed that one (98CM19) was a complex mosaic between subtype A in p24 and subtype J prot, and unclassifiable in env (C2V3 or ***gp41***). The second, 98CM63, clustered distinctly from all known subtypes in p24, prot, C2V3, or ***gp41*** . 98CM63 clustered with a specimen from Cyprus and these two geographically and epidemiologically unlinked specimens, with their distinct clustering pattern, may represent a new subcluster of subtype A. In conclusion, these findings confirm the high ***HIV*** - ***1*** genetic variability and further suggest the continuous appearance of new viral strains in this population.

L24 ANSWER 2 OF 21 MEDLINE
2000425604 Document Number: 20342568. Serological detection of infection with diverse human and simian immunodeficiency viruses using consensus env peptides. Masciotra S; Rudolph D L; van der Groen G; Yang C; Lal R B. (HIV

Immunology and Diagnostics Branch, Division of AIDS, STD, and TB Laboratory Research, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333, USA.) CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, (2000 Jul) 7 (4) 706-9. Journal code: CB7. ISSN: 1071-412X. Pub. country: United States. Language: English.

AB Cross-species transmission has been shown to play an important role in the emergence of human retroviruses. We developed a generic enzyme immunoassay using synthetic peptides from ***gp41*** and C2V3 consensus sequences (human immunodeficiency virus [HIV] type 1 [***HIV*** - ***1***] groups M, O, and N and the homologous region of simian immunodeficiency virus [SIV] strains from chimpanzees [SIVcpz], SIVcpzGAB1 and SIVcpzANT) to detect divergent HIV and SIV. A cocktail of peptides from ***gp41*** and C2V3 (M-O) detected all ***HIV*** - ***1*** group M and O sera and showed cross-reactivity with SIVcpz sera. Further, a mixture of C2V3 peptides (GAB1-ANT) failed to detect ***HIV*** - ***1*** infections but reacted with all SIVcpz sera, allowing discrimination of SIVcpz from ***HIV*** - ***1*** infections. Since most SIVcpz sera cross-reacted with ***HIV*** - ***1*** peptides, we next evaluated SIVcpz serum reactivity with rapid tests for ***HIV*** - ***1*** /2. SIVcpzANT and SIVcpzUS sera reacted with the Sero-strip and Multispot assays. Both tests are sensitive in detecting group M (97 100%, respectively), although Multispot has lower sensitivity for ***group*** ***O*** detection (67%) than does Sero-strip (100%). The limited volume and time required to perform these assays make them a generic tool for field screening. The env peptide-based assay and rapid tests should allow for the identification of emerging variants of HIV and SIV.

L24 ANSWER 6 OF 21 MEDLINE
2000122461 Document Number: 20122461. Analysis of genetic variability within the immunodominant epitopes of envelope ***gp41*** from ***human*** ***immunodeficiency*** ***virus*** ***type*** ***1*** (***HIV*** - ***1***) group M and its impact on ***HIV*** - ***1*** antibody detection. Dorn J; Masciotra S; Yang C; Downing R; Biryahwaho B; Mastro T D; Nkengasong J; Pieniazek D; Rayfield M A; Hu D J; Lal R B. (HIV Immunology and Diagnostics Branch, National Center for HIV, STD and TB Prevention, Centers for Disease Control and Prevntion, Atlanta, Georgia 30333, USA.) JOURNAL OF CLINICAL MICROBIOLOGY, (2000 Feb) 38 (2) 773-80. Journal code: HSH. ISSN: 0095-1137. Pub. country: United States. Language: English.

AB The serodiagnosis of ***human*** ***immunodeficiency*** ***virus*** ***type*** ***1*** (***HIV*** - ***1***) infection primarily relies on the detection of antibodies, most of which are directed against the immunodominant regions (IDR) of ***HIV*** - ***1*** structural proteins. Among these, the N-terminal region of ***gp41*** contains cluster I (amino acids [aa] 580 to 623), comprising the cytotoxic T-lymphocyte epitope (AVERYLKDQQLL) and the cysteine loop (CSGKLIC), and cluster II (aa 646 to 682), comprising an ectodomain region (ELDKWA). To delineate the epitope diversity within clusters I and II and to determine whether the diversity affects serologic detection by U.S. Food and Drug Administration (FDA)-licensed enzyme immunoassay (EIA) kits, ***gp41*** Env sequences from 247 seropositive persons infected with ***HIV*** - ***1*** group M, subtypes A (n = 42), B (n = 62), B' (n = 13), C (n = 38), D (n = 41), E (n = 18), F (n = 27), and G (n = 6), and 6 ***HIV*** - ***1*** -infected but persistently seronegative (HIPS) persons were analyzed. While all IDR were highly conserved among both seropositive and HIPS persons, minor amino acid substitutions (<20% for any one residue, mostly conservative) were observed for all subtypes, except for B', in comparison with the consensus sequence for each subtype.

Most importantly, none of the observed substitutions among the group M plasma specimens affected antibody detection, since all specimens (n = 152) tested positive with all five FDA-licensed EIA kits. Furthermore, all specimens reacted with a group M consensus ***gp41*** peptide (WGIKQLQARVLAVERYLKDQQLLGIWGCSGKLICTTAVPWNASW), and high degrees of cross-reactivity (>80%) were observed with an ***HIV*** - ***1*** group N peptide, an ***HIV*** - ***1*** ***group*** ***O*** peptide, and a peptide derived from the homologous region of ***gp41*** from simian immunodeficiency virus from chimpanzee (SIVcpz). Taken together, these data indicate that the minor substitutions observed within the IDR of ***gp41*** of ***HIV*** - ***1*** group M subtypes do not affect antibody recognition and that all ***HIV*** - ***1*** -seropositive specimens containing the observed substitutions react with the FDA-licensed EIA kits regardless of viral genotype and geographic origin.

L24 ANSWER 7 OF 21 MEDLINE
1999284364 Document Number: 99284364. Phylogeny of HIV type 1 ***group*** ***O*** isolates based on env gene sequences. Mas A; Quinones-Mateu M E; Domingo E; Soriano V. (Centro de Biologia Molecular Severo Ochoa, UAM, Cantoblanco, Madrid, Spain.) AIDS RESEARCH AND HUMAN RETROVIRUSES, (1999 May 20) 15 (8) 769-73. Journal code: ART. ISSN: 0889-2229. Pub. country: United States. Language: English.

L24 ANSWER 10 OF 21 MEDLINE
1998435941 Document Number: 98435941. Molecular characterization of the envelope transmembrane glycoprotein of 13 new ***human*** ***immunodeficiency*** ***virus*** ***type*** ***1*** ***group*** ***O*** strains from six different African countries. Bibollet-Ruche F; Peeters M; Mboup S; Ekaza E; Gandji R; Torimiro J; Mpoudi E N; Amblard J; Dibanga G; Saidou M; Esu-Williams E; Vanden Haesevelde M; Saman E; Delaporte E. (Project SIDAK, Laboratoire Retrovirus, ORSTOM, Montpellier, France.) AIDS RESEARCH AND HUMAN RETROVIRUSES, (1998 Sep 20) 14 (14) 1281-5. Journal code: ART. ISSN: 0889-2229. Pub. country: United States. Language: English.

L24 ANSWER 11 OF 21 MEDLINE
1998074180 Document Number: 98074180. Serologic and phylogenetic characterization of ***HIV*** - ***1*** subtypes in Uganda. Brennan C A; Lund J K; Golden A; Yamaguchi J; Vallari A S; Phillips J F; Kataaha P K; Jackson J B; Devare S G. (Abbott Laboratories, North Chicago, Illinois 60064, USA.) AIDS, (1997 Dec) 11 (15) 1823-32. Journal code: AID. ISSN: 0269-9370. Pub. country: United States. Language: English.

AB OBJECTIVES: To determine the HIV genetic subtypes present in ***HIV*** - ***1*** -infected asymptomatic blood donors in Uganda and to evaluate serologic detection of infection by commercial immunoassays; to evaluate samples for ***HIV*** - ***1*** ***group*** ***O*** infections. METHODS: Sixty-four HIV-seropositive plasma samples were collected from the Nakasero Blood Bank, Kampala, Uganda. The plasma were evaluated using commercial HIV enzyme immunoassays (EIA) and a research immunoblot. ***HIV*** - ***1*** group M and O infections were identified on the basis of discordant seroreactivity in EIA and reactivity to group M and O antigens on the immunoblot. Regions of gag p24 and env ***gp41*** were amplified using reverse transcriptase polymerase chain reaction, and genetic subtypes were determined by phylogenetic analysis. RESULTS: Serologic testing confirmed that 63 out of 64 plasma units were positive for ***HIV*** - ***1*** group M infection and showed no evidence of ***HIV*** - ***1*** ***group*** ***O*** infections. Genetic subtyping determined that 25 samples were subtype A, three subtype C, 22 subtype D, and nine were heterogeneous for subtypes A

and D. CONCLUSIONS: Despite the sequence variation observed in Uganda, commercial EIA based on ***HIV*** - ***1*** subtype B proteins detected all the infections. In contrast, a peptide-based assay failed to detect three infections by subtype D viruses. This emphasizes the negative impact of HIV genetic variation on assays that rely on peptides to detect HIV infections. The number of infections with heterogeneous subtype (due to mixed infections or recombinant viruses) is high and reflects the growing complexity of the HIV epidemic in endemic regions where multiple subtypes are present in the population.

L24 ANSWER 14 OF 21 MEDLINE
97407536 Document Number: 97407536. Synthetic peptide ELISAs for detection of and discrimination between group M and ***group*** ***O*** HIV type 1 infection. Maucl`ere P; Damond F; Apetrei C; Loussert-Ajaka I; Souqui`ere S; Buzelay L; Dalbon P; Jolivet M; Mony Lobe M; Brun-Vezinet F; Simon F; Barin F. (Laboratoire National de Sante Publique et de Reference, Centre Pasteur, Yaounde, Cameroon.) AIDS RESEARCH AND HUMAN RETROVIRUSES, (1997 Aug 10) 13 (12) 987-93. Journal code: ART. ISSN: 0889-2229. Pub. country: United States. Language: English.

AB We developed and evaluated two peptide-based immunoassays to confirm and discriminate between group M and ***group*** ***O*** ***HIV*** - ***1*** infection. These assays are based on in vitro competition for antibody binding between M and O peptides. The first EIA is based on competition between group M and ***group*** ***O*** ***gp41*** immunodominant domains and the second on competition between ***group*** ***O*** and group M V3 regions of gp120. Two panels of sera were used: the first consisted of 109 sera collected from 27 ***group*** ***O*** - and 92 group M-infected patients in whom the HIV isolates had been genotyped by sequencing or heteroduplex mobility assay. In this panel, the combination of the two assays correctly discriminated 106 samples (100% ***group*** ***O*** and 96.7% group M samples). The second panel, used for the field evaluation of the two assays, consisted of 157 samples from ***HIV*** - ***1*** -infected Cameroonian patients, 33 strains having been genotyped. The combination of the two techniques in a serogrouping algorithm discriminated 147 of these samples, 74 being ***HIV*** - ***1*** ***group*** ***O*** and 73 group M. These results always correlated with genotyping results. The 10 sera that were not successfully classified by these assays were from early seroconverters. Altogether, the two assays clearly differentiated 263 of 276 (94.9%) samples in the two panels. On the basis of the genotyping results, the positive predictive value for group discrimination in the two panels was 100% for both GSEIA assays. Our peptide-blocking group-specific EIAs for differentiation and confirmation of ***HIV*** - ***1*** group M and ***group*** ***O*** infection are complementary tools for epidemiological studies and surveillance of ***HIV*** - ***1*** ***group*** ***O*** strain trafficking.

L25 ANSWER 59 OF 65 MEDLINE
87149036 Document Number: 87149036. Mechanisms of antibody binding to a protein. Getzoff E D; ***Geysen H M*** ; Rodda S J; Alexander H; Tainer J A; Lerner R A. SCIENCE, (1987 Mar 6) 235 (4793) 1191-6. Journal code: UJ7. ISSN: 0036-8075. Pub. country: United States. Language: English.

AB The mechanisms of antibody binding to a protein were studied by an analysis of specific amino acid residues critical to nine antigenic sites on myohemerythrin. Rabbit antisera to the whole protein were assayed for binding to more than 1500 distinct peptide analogs differing from the protein sequence by single amino acid replacements. The results, combined with information from the three-dimensional crystallographic structure, were used to evaluate probable mechanisms of antibody binding at

individual sites. The data from all sites examined indicate that initial binding to solvent-exposed amino acid residues may promote local side-chain displacements and thereby allow the participation of other, previously buried, residues.

L25 ANSWER 58 OF 65 MEDLINE
88009183 Document Number: 88009183. Strategies for epitope analysis using peptide synthesis. ***Geysen H M*** ; Rodda S J; Mason T J; Tribbick G; Schoofs P G. (Department of Molecular Immunology, Commonwealth Serum Laboratories, Parkville, Victoria, Australia..) JOURNAL OF IMMUNOLOGICAL METHODS, (1987 Sep 24) 102 (2) 259-74. Journal code: IFE. ISSN: 0022-1759. Pub. country: Netherlands. Language: English.

AB A recently developed approach to the synthesis and ELISA screening of large numbers of peptides is described. The method has created the opportunity to tackle questions about the sites and specificity of antigenic determinants which were formerly thought to be too difficult to answer. The various strategies for application of this method are described along with examples of their successful use. They include a procedure for locating all the continuous antigenic peptides of a protein antigen, and the identification of non-replaceable amino acid residues within an antigenic peptide. An approach to the determination of amino acid residues involved in the epitope for any monoclonal antibody is also described. These strategies open up the prospect of rapid mapping of the antigenic properties of hitherto poorly understood antigens.

L25 ANSWER 57 OF 65 MEDLINE
88068630 Document Number: 88068630. Influence of protein flexibility and peptide conformation on reactivity of monoclonal anti-peptide antibodies with a protein alpha-helix. Fieser T M; Tainer J A; ***Geysen H M*** ; Houghten R A; Lerner R A. (Department of Molecular Biology, Research Institute of Scripps Clinic, La Jolla, CA 92037.) PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1987 Dec) 84 (23) 8568-72. Journal code: PV3. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB Monoclonal antibodies against an alpha-helical region of the iron-containing, oxygen-binding protein myohemerythrin were isolated following immunization of mice with either the whole protein or a peptide homolog of the helix. Three distinct epitopes within the myohemerythrin helix were identified. The individual residues within two of these epitopes that were essential for antibody binding were determined by measuring antibody binding to a set of peptides in which each amino acid of the epitope was replaced in turn by each of the other 19 amino acids. Hydrophilic residues that are exposed in the native conformation and buried, hydrophobic residues were both shown to be irreplaceable, suggesting their direct involvement in antibody binding. The influence of antigen conformation on antibody binding to these amphipathic epitopes was assessed by measuring the relative affinities of the antibodies for peptides, intact protein, and apoprotein. All of the antibodies bound to apoprotein better than to native protein, indicating that relaxation of the native structure by removal of the iron center increases antibody affinity for myohemerythrin. However, not all of the antibodies tested bound to peptides better than to protein, suggesting that increased antigen flexibility is not always sufficient to maximize antibody binding. Antibody binding to peptides appeared to also be influenced by the ability of the peptides to attain secondary structure at the epitopes, either alone or due to carrier influences.

L25 ANSWER 56 OF 65 MEDLINE
88088881 Document Number: 88088881. Epitopes of an influenza viral peptide

recognized by antibody at single amino acid resolution. Schoofs P G; ***Geysen H M*** ; Jackson D C; Brown L E; Tang X L; White D O. (Department of Molecular Immunology, Commonwealth Serum Laboratories, Parkville, Victoria, Australia.) JOURNAL OF IMMUNOLOGY, (1988 Jan 15) 140 (2) 611-6. Journal code: IFB. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Antibodies raised against the synthetic peptide corresponding to the carboxy-terminal 24 amino acids (305-328) of the heavy chain of the hemagglutinin molecule of influenza virus A/X-31 (H3) bind this peptide at three antigenic sites. These sites were identified by assaying binding of polyclonal BALB/c mouse antipeptide sera to the complete set of all possible di-, tri, tetra-, penta-, hexa-, hepta-, and octapeptides homologous with the 24-residue sequence. Individual epitopes were defined and essential residues identified by testing the binding of monoclonal antibodies to sets of peptide analogues in which every one of the homologous residues was replaced in turn by each of the 19 alternative genetically coded amino acids. The immunodominant epitope was shown to be a linear sequence of five amino acids, 314LKLAT318. **Replacement of any one of these residues with any other amino acid resulted in loss of antibody binding, indicating that all five are essential to the interaction and that they are probably contact residues**. Another antigenic site contains at least two overlapping epitopes: polyclonal sera recognize predominantly an epitope or epitopes encompassed by the linear sequence 320MRNVPEKQT328, whereas the epitope defined by a particular monoclonal antibody comprises the seven amino acids 322NVPEKQT328, of which N322, E325, and Q327 were implicated as contact residues.

L25 ANSWER 54 OF 65 MEDLINE
89046801 Document Number: 89046801. The chemistry and mechanism of antibody binding to protein antigens. Getzoff E D; Tainer J A; Lerner R A; ***Geysen H M*** . (Department of Molecular Biology, Research Institute of Scripps Clinic, La Jolla, California 92037.) ADVANCES IN IMMUNOLOGY, (1988) 43 1-98. Ref: 269. Journal code: 2N9. ISSN: 0065-2776. Pub. country: United States. Language: English.

L25 ANSWER 47 OF 65 MEDLINE
90234496 Document Number: 90234496. Cognitive features of continuous antigenic determinants [published erratum appears in J Mol Recognit 1989 Jul;2(1):49]. ***Geysen H M*** ; Mason T J; Rodda S J. (Department of Molecular Immunology, Commonwealth Serum Laboratories, Parkville, Victoria, Australia..) JOURNAL OF MOLECULAR RECOGNITION, (1988 Feb) 1 (1) 32-41. Journal code: A00. ISSN: 0952-3499. Pub. country: ENGLAND: United Kingdom. Language: English.

AB We sought to identify the features controlling the specificity of antibody recognition and thus gain insights into molecular recognition between proteins in general. A total of 103 epitopes within 63 well-defined antigenic peptides homologous with the relevant antigen sequence were identified. The contribution of each amino acid residue to the antibody binding activity of each epitope was investigated by ELISA testing of complete sets of peptide analogs containing single amino acid replacements. The data are summarized in a replaceability matrix. Some of the high frequency replaceabilities were expected, such as aspartate for glutamate, serine for threonine, etc., but unexpected relationships were also found, such as a high degree of acceptability of methionine as a replacement. Replaceability with a residue of opposite charge was rare. Glycine and tyrosine were frequently of low acceptability, except for glycine as a replacement for alanine. It was found that on average only about four to five amino acid residues in epitopes were required to

determine specificity and provide binding energy. Specificity and binding energy were attributed to amino acid side chains rather than main chain atoms. Propensity factors for occurrence of amino acids in antigenic determinants were calculated. The prominence of certain hydrophobic residues as residues critical to recognition by antibody suggests that the molecular surface of an antigen in its combined form with antibody is altered from that occurring in the absence of antibody. Thus, antigenicity is not a static surface phenomenon but depends on the ability of the antigen to undergo rearrangement, supporting the induced fit concept.

L25 ANSWER 33 OF 65 MEDLINE
92013053 Document Number: 92013053. Role of single amino acids in the recognition of a T cell epitope. Suhrbier A; Rodda S J; Ho P C; Csurhes P; Dunckley H; Saul A; ***Geysen H M*** ; Rzepczyk C M. (Queensland Institute of Medical Research, Brisbane, Australia..) JOURNAL OF IMMUNOLOGY, (1991 Oct 15) 147 (8) 2507-13. Journal code: IFB. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB T cell epitopes can be defined by the use of synthetic peptides, which when added to APC efficiently mimic naturally processed Ag. Free peptide is thought to bind to cell-surface MHC glycoproteins and the TCR then recognizes the resulting complex. The specificity of a tetanus toxin-specific human Th cell clone was investigated using a complete replacement set of peptides in which every amino acid within the minimal T cell epitope was replaced by each of the 19 alternative genetically coded amino acids. Within the minimal epitope, found to be YSYFPSVI (tetanus toxin 593-600), a small number of substitutions could be made without significant loss of activity, defined as substitutions giving peptides whose activity fell within +/- 3 SD of the mean parent response. Y593 could be substituted with F, W, M, L, V, and I; S594 with G and T; Y595, F596, and P597 with no other amino acids; S598 with A; V599 with S, and I600 with L. Rank ordering of the substitutions allowed a precise description to be made of MHC and/or TCR interaction with each amino acid side chain within the epitope. Simplified theoretic calculations based on this study indicate that class II T cell recognition has a specificity greater than 1 in 10(8). Competition experiments indicate that Y595, F596, P597, and I600 are critical for binding of this epitope to its restricting element, HLA DR4Dw14.

L25 ANSWER 25 OF 65 MEDLINE
92228783 Document Number: 92228783. Altering the antigenicity of proteins. Alexander H; Alexander S; Getzoff E D; Tainer J A; ***Geysen H M*** ; Lerner R A. (Division of Biological Sciences, University of Missouri, Columbia 65211.) PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1992 Apr 15) 89 (8) 3352-6. Journal code: PV3. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB To better understand the binding interaction between antigen and antibody we need to distinguish protein residues critical to the binding energy and mechanism from residues merely localized in the interface. By analyzing the binding of monoclonal antibodies to recombinant wild-type and mutant myohemerythrin (MHr) proteins, we were able to test the role of individual critical residues at the highly antigenic site MHr-(79-84), within the context of the folded protein. The results directly show the existence of antigenically critical residues, whose mutations significantly reduce antibody binding to the folded protein, thus verifying peptide-based assignments of these critical residues and demonstrating the ability of buried side chains to influence antigenicity. Taken together, these results (i) distinguish the antigenic surface from the solvent-exposed protein surface before binding, (ii) support a two-stage interaction mechanism allowing inducible changes in protein antigens by antibody

binding, and (iii) show that **protein antigenicity can be significantly reduced by alteration of single critical residues without destroying biological activity.**

L25 ANSWER 22 OF 65 MEDLINE
92369705 Document Number: 92369705. Effects of end groups on the stimulatory capacity of minimal length T cell determinant peptides. Mutch D A; Rodda S J; Benstead M; Valerio R M; ***Geysen H M*** . (Coselco Mimotopes Pty. Ltd., Clayton, Victoria, Australia..) PEPTIDE RESEARCH, (1991 May-Jun) 4 (3) 132-7. Journal code: BE1. ISSN: 1040-5704. Pub. country: United States. Language: English.

AB We studied the effect of end groups on the capacity of two closely related peptides to stimulate a human T cell clone. Using multipin peptide synthesis technology, we generated solution phase peptides with six combinations of end groups for each sequence. The end modifications examined were amino-terminal acetylation, carboxy-terminal methylamidation or the addition of a dipeptide containing a diketopiperazine ring. The response to the less stimulatory of the two peptide sequences was significantly increased by acetylation of the amino-terminus, a finding which was consistent at different peptide doses. Amino-terminal acetylation was found to be more significant in affecting responses than any of the carboxy-terminal modifications tested. The use of peptides with a diketopiperazine ring structure at the carboxy-terminus did not interfere with presentation and recognition of peptides and may enhance the effectiveness of peptides for T cell epitope scanning.

L28 ANSWER 1 OF 2 MEDLINE
93135927 Document Number: 93135927. Fine specificity of antibody recognition of carcinoma-associated epithelial mucins: antibody binding to synthetic peptide epitopes. Briggs S; Price M R; Tendler S J. (Cancer Research Campaign Laboratories, University of Nottingham, U.K..) EUROPEAN JOURNAL OF CANCER, (1993) 29A (2) 230-7. Journal code: ARV. ISSN: 0959-8049. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The protein core of polymorphic epithelial mucins consists predominantly of a repeating 20 amino acid peptide motif. Many monoclonal antibodies reactive with breast carcinomas recognise determinants located within the mucin protein core, and ***epitope*** mapping techniques have demonstrated that these antibodies bind to epitopes of three, four or five amino acids within the hydrophilic sequence, P D T R P A P. Each of these mucin core-reactive antibodies map to epitopes containing the central arginine residue. The fine specificity of a panel of anti-mucin antibodies binding to the tetrameric peptides P D T R or R P A P (synthesised on the heads of polyethylene pins) was examined by systematically replacing each amino acid in turn with all other 19 natural amino acids, and then testing these analogues for antibody binding. We have (i) identified those amino acids in epitopes which are essential for antibody binding, (ii) shown that for each ***epitope*** there is a hierarchy of residues required for immune recognition--certain amino acids may be ***replaced*** with little or no ***loss*** of ***antibody*** ***binding*** , while the presence of others is essential, and (iii) concluded that antibody specificity is further regulated by the residue(s) flanking an ***epitope*** motif which may impose conformational constraints upon the presentation of the ***epitope*** to an antibody.

L29 ANSWER 98 OF 110 MEDLINE
90038509 Document Number: 90038509. Sequences outside a minimal immunodominant site exert negative effects on recognition by staphylococcal nuclease-specific T cell clones. Vacchio M S; Berzofsky J A; Krzych U; Smith J A; Hodes R J; Finnegan A. (Experimental Immunology

Branch, National Cancer Institute, Bethesda, MD 20892..) JOURNAL OF IMMUNOLOGY, (1989 Nov 1) 143 (9) 2814-9. Journal code: IFB. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB In recent years, synthetic peptides have been utilized extensively to characterize the minimal essential immunodominant sites on model protein Ag. However, little work has focused on the effect that sequences ***flanking*** these minimal recognition sites may exert on T cell recognition. Previous work with staphylococcal nuclease (Nase) demonstrated that I-Ek-restricted clones recognize the peptide 81-100, whereas I-Ab-restricted clones recognize the over-lapping but non-cross-reacting peptide 91-110. Further analysis with 15 or 10 residue peptides within the region 81-110 reveals that the minimal sequence capable of stimulating I-Ek-restricted clones is contained within the decapeptide 91-100. Addition of residues 86-90, to give the peptide 86-100, enhanced the recognition substantially, whereas addition of residues 101-105 produced a 91-105 peptide with no stimulatory ability. These results suggest that interactions between the ***antigenic*** peptide 91-100 and residues within the ***flanking*** 101-105 sequence have negative consequences for presentation of the immunodominant ***epitope*** to T cell clones. Introduction of single amino acid ***substitutions*** within 91-105 produced peptides that induce responses comparable to those seen with 91-100. These results are consistent with the suggestion of negative interactions between the minimal immunodominant site and ***flanking*** sequences in that single residue ***substitutions*** may remove these negative interactions and lead to restoration of stimulatory ability. The negative effect of ***flanking*** sequences on T cell recognition of immunodominant sites presents new considerations for development of synthetic vaccines as well as for understanding the biology of Ag processing and presentation.

L29 ANSWER 91 OF 110 MEDLINE
91056552 Document Number: 91056552. Analysis of sequence diversity in hypervariable regions of the external glycoprotein of human immunodeficiency virus type 1. Simmonds P; Balfe P; Ludlam C A; Bishop J O; Brown A J. (Department of Genetics, University of Edinburgh, Scotland.) JOURNAL OF VIROLOGY, (1990 Dec) 64 (12) 5840-50. Journal code: KCV. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB Nucleotide sequences in three hypervariable regions of the human immunodeficiency virus type 1 (HIV-1) env gene were obtained by sequencing provirus present in peripheral blood mononuclear cells of HIV-infected individuals. Single molecules of target sequences were isolated by limiting dilution and amplified in two stages by the polymerase chain reaction, using nested primers. The product was directly sequenced to avoid errors introduced by Taq polymerase during the amplification process. There was extensive variation between sequences from the same individual as well as between sequences from different individuals. Interpatient variability was markedly less in individuals infected from a common source. A high proportion of amino acid ***substitutions*** in the hypervariable regions altered the number and positions of potential N-linked glycosylation sites. Sequences in two hypervariable regions frequently contained short (3- to 15-bp) duplications or deletions, and by amplifying peripheral blood mononuclear cell DNA containing 10(2) or 10(3) proviral molecules and analyzing the product by high-resolution electrophoresis, the total number and abundance of distinct length variants within an individual could be estimated, providing a more comprehensive analysis of the variants present than would be obtained by sequencing alone. Sequences from many individuals showed frequent amino acid ***substitutions*** at certain key positions for

neutralizing-antibody and cytotoxic T-cell recognition in the immunodominant loop. The rates of synonymous and nonsynonymous nucleotide substitution in the region of this and ***flanking*** regions indicate that strong positive selection for amino acid change is operating in the generation of ***antigenic*** diversity.

L29 ANSWER 88 OF 110 MEDLINE
92014073 Document Number: 92014073. Monoclonal antibodies against myelin proteolipid protein: identification and characterization of two major determinants. Yamamura T; Konola J T; Wekerle H; Lees M B. (Biochemistry Division, E.K. Shriver Center, Waltham, MA 02254..) JOURNAL OF NEUROCHEMISTRY, (1991 Nov) 57 (5) 1671-80. Journal code: JAV. ISSN: 0022-3042. Pub. country: United States. Language: English.

AB This report describes the preparation and characterization of a panel of monoclonal antibodies (mAbs) against the myelin proteolipid protein (PLP). A Lewis rat was immunized with bovine proteolipid apoprotein and 27 mAbs were selected based on their reactivity against bovine PLP on enzyme-linked immunosorbent assays. Eleven mAbs recognized the PLP carboxyl-terminal sequence when tested against a panel of synthetic peptides in a solid-phase assay. A carboxyl-terminal pentapeptide (residues 272-276) was sufficient for antibody binding and the terminal phenylalanine residue was found particularly important. **Deletion, modification, or ***replacement*** of this residue markedly reduced or obliterated ***antigen*** -antibody interaction**. Nine mAbs reacted with a second ***antigenic*** determinant, residues 209-217, but these could be identified only by competitive immunoassays. This peptide was a more effective inhibitor than the longer peptides 202-217 and 205-221, suggesting that *****flanking*** residues may interfere with peptide-antibody interaction**. Seven antibodies did not react with any of the synthetic peptides tested and their determinants remain unidentified. Immunoblot analysis showed that the mAbs reacted with both the PLP and the DM-20 isoforms. Twenty-three of the mAbs were of the immunoglobulin G2a or b isotype; the remaining antibodies were immunoglobulin M and all of these were specific for residues 209-217. Cultured murine oligodendrocytes were stained by most of the mAbs tested, but the most intense reactivity was observed with the carboxyl-terminus-specific mAbs. The immunocytochemical analyses demonstrate that the mAbs react with the native PLP in situ and show their potential usefulness for studies of the cell biology of myelin and oligodendrocytes.

L29 ANSWER 78 OF 110 MEDLINE
92348189 Document Number: 92348189. In vitro mutagenesis of HLA-B27: single and multiple amino acid ***substitutions*** at consensus B27 sites identify distinct monoclonal antibody-defined epitopes. el-Zaatari F A; Taurog J D. (Harold C. Simmons Arthritis Research Center, University of Texas Southwestern Medical Center, Dallas 75235-8884..) HUMAN IMMUNOLOGY, (1992 Apr) 33 (4) 243-8. Journal code: G9W. ISSN: 0198-8859. Pub. country: United States. Language: English.

AB The consensus HLA-B27 sequence includes a unique constellation of amino acid residues along the peptide-binding cleft. To investigate the potential role of this region in the ***antigenic*** structure of HLA-B27, a panel of transfected cell lines was produced expressing 24 mutant B27 molecules with single or multiple ***substitutions*** within this constellation of residues. The cells were analyzed by flow cytometry with a panel of four anti-B27 mAb: ME1, GSP5.3, GS145.2, and B27M2. Previous studies have suggested that position 67 exerts a conformational effect on the ME1, GSP5.3, and GS145.2 epitopes. This was further supported in these studies by the observation that additional

substitutions at the ***flanking*** residues 63 and 70 could reverse the disruption of these mAb epitopes by large residues at 67.

*****Substitutions*** at positions 69-71 disrupted the binding of ME1 and GSP5.3, apparently by a direct effect.** Individual ***substitutions*** at either of the two positions bearing residues unique to B27, 70 and 97, had no significant influence on the binding of any of the four mAb. The region of amino acid positions 63-71 in HLA-B27 thus appears to participate in the formation of at least three distinct epitopes shared by B27 and B7, identified by ME1, GSP5.3, and GS145.2.